510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY AND INSTRUMENT COMBINATION TEMPLATE

A. 510(k) Number:

k051651

B. Purpose for Submission:

New Device

C. Measurand:

Glucose

D. Type of Test:

Quantitative; electrochemical biosensor

E. Applicant:

US Diagnostics, Inc.

F. Proprietary and Established Names:

G4 Blood Glucose Monitoring System, G4 Test Strips and G4 Control Solutions.

G. Regulatory Information:

1. Regulation section:

   21 CFR 862.1345, Glucose Test System

   21 CFR 862.1660, Quality Control Material (assayed and unassayed)

2. Classification:

   Class II (glucose test system)

   Class I, reserved (controls)

3. Product code:

   NBW, System Test, Blood Glucose, Over the Counter

CGA, Glucose Oxidase, Glucose

JJX, Single (Specified) Analyte Controls (Assayed and Unassayed)

4. Panel:

   75, Chemistry

H. Intended Use:

1. Intended use(s):
   See indications for use below.

2. Indication(s) for use:

   The G4™ Meter Device is used for the quantitative measurement of glucose level in capillary whole blood as an aid in monitoring the effectiveness of diabetes management in the home and in clinical settings. G4™ System is for testing outside the body (in vitro diagnostic use only). Testing sites include the traditional fingertip testing along with alternate site testing on the arm.

   The G4™ Test Strips are used for the quantitative measurement of glucose level in whole blood as an aid in monitoring the effectiveness of diabetes management in the home and in clinical settings. G4™ System is for testing outside the body (in vitro diagnostic use only). Testing sites include the traditional fingertip testing along with alternate site testing on the arm.

   The G4™ Control Solutions are a red liquid which is to be used to check that both the G4™ meter and G4™ test strips are working together properly. It contains a known range of glucose as specified on the vial.

3. Special conditions for use statement(s):

   Capillary blood testing sites for this device are fingertip and forearm.

   Forearm results may be different from fingertip results when glucose levels are changing rapidly (e.g., after eating a meal, taking insulin, or during or after exercise).
   Users are cautioned they should not use the forearm, they should use their fingertips if:
   A. They think their blood sugar is low (hypoglycemia),
   B. They have been diagnosed with hypoglycemic unawareness, or
   C. The results from the forearm do not agree with the way they feel.

4. Special instrument requirements:

   The G4™ Meter Device

I. Device Description:

The G4 Meter Device is comprised of the G4 Glucose Meter, G4 Test Strips, check strips, lancing device, lancets, G4 control solution, user manual, quick reference guide and a logbook.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Lifescan, Inc. SureStep, Lifescan, Inc. Ultra, and Roche Diagnostics Accu-Chek

2. Predicate 510(k) number(s):

   k984261, k024194, and k021513 respectively

3. Comparison with predicates:

Similarities		
Item	Device	Predicate
Enzyme	Glucose Oxidase	Glucose Oxidase
Mediator	Hexaaminеruthenium(III) chloride	
Electrode	Carbon	Carbon

Differences		
Item	Device	Predicate
Range	20 to 600 mg/dL	0 to 600 mg/dL
Hematocrit	20 to 60 %	20 to 65%
Test Time	5 seconds	15 seconds
Sample Size	0.5 uL	2 uL
Humidity Range	35 - 85%	<85%
Memory Capacity	250 Tests	150 Tests
Power	3.0 V	5.0 V
Dimensions	~99 mm x 47 mm x 15.5 mm	~ 91 mm x 82 mm x 18 mm

K. Standard/Guidance Document Referenced (if applicable):

ISO Document 15197- In vitro diagnostic test systems- Requirements for blood-glucose monitoring systems for self-testing in managing diabetes mellitus.

L. Test Principle:

The G4 Meter Device system employs a disposable reagent strip technology, based on the glucose oxidase method for glucose determination. Each test strip features an electrode

containing the enzyme glucose oxidase. A blood sample is applied to the blood collection area at the tip of the strip and is automatically drawn into the reaction zone, where the glucose oxidase catalyzes the oxidation of glucose to produce gluconic acid. During the reaction, a mediator transfers electrons to the electrode surface and generates a current. The amount of the current is proportional to the amount of glucose present in the blood sample.

M. Performance Characteristics (if/when applicable):

The sponsor conducted performance studies according to ISO 15197 (see section K above).

1. Analytical performance:

a. Precision/Reproducibility:

Intermediate precision testing was conducted with 3 levels of glucose prepared from control solutions. Each sample was measured daily for 12 days using ten meters across multiple strip lots (each assigned a meter). The glucose concentration ranges were 30 to 50 mg/dL, 96 to 144 mg/dL and 280 to 420 mg/dL. The results are shown in the chart below.

Range (mg/dL)	N	Mean (mg/dL)	SD	CV %
30-50	120	44.1	2.2	4.9
96-144	120	134.9	5.9	4.4
280-420	120	353.6	18.6	5.2

b. Linearity/assay reportable range:

A linearity study was conducted by comparing nine prepared whole blood samples on the G4 test strip (one lot) and a glucose reference method (YSI 2300 STAT Plus) that spanned the range of 15 to 710 mg/dL. The mean value of each aliquot was calculated. The linear regression equation for the linear regression analysis of results form the G4 device and the YSI method was Y= 1.0x – 17.976 with an R of 0.993. The measuring range is 20 to 600 mg/dL.

c. Traceability, Stability, Expected values (controls, calibrators, or methods):

The sponsor conducted both a real time shelf-life and use time (open vial) stability study for the G4 Control solutions. The real-time shelf-life stability study was evaluated every 60 to 120 days for 540 days. The use time stability study was evaluated every 7 to 10 days for 90 days. Both studies were conducted in a cool, dry place with a temperature of 8 to 30° C.

Real-time shelf-life studies performed by the manufacturer indicate that unopened G4 Control Solutions have a shelf-life period of 18 months and a use- life (open-vial) of 3 months.

The G4 test strips were evaluated for shelf-life stability (closed vial) in an accelerated study. A continuing real-time study is being conducted on three lots that are tested weekly for 540 days. The accelerated study shows stability of 18 months for unopened test strips and 3 months for open test strips.

Value assignments for three lots of both levels of control solutions (6 lots total) were determined using 5 replicates of one test strip lot read on a G4 meter.

d. Detection limit:

The low and high detection limits for the G4 Meter Device have been set at 20 and 600 mg/dL. Readings below or above these values will generate a "Lo" or "Hi" result respectively.

e. Analytical specificity:

An interference study that evaluated heparinized whole blood samples was conducted with the G4 device. The YSI 2300 STAT Plus was used as the reference method. Two interferent levels were tested (n=5) in two blood glucose concentrations (~ 87 and 200 mg/dL) with one lot of test strips. The difference, average, standard deviation, CV and % bias were calculated and the interference results met the sponsor's acceptance criteria. Interferences were tested at two levels shown in the chart below.

Generic name	Therapeutic level	Toxic level	Test level 1	Test level 2
Ascorbic acid	8 – 12	NA	free	30
Acetaminophen	10 - 20	150	free	20
Uric acid	Men: 45 – 80 women: 25 – 62		free	80
Bilirubin	20		free	20
Dopamine	-	-	free	15
L-dopa	-	-	free	5
Methyldopa	0.1~0.5	1	free	3
Tolbutamide	5.3~10	64	free	150
Triglycerides	3000	-	free	3000

Based upon the studies above, the sponsor is adding the following to the package insert:

- Blood samples that contain large amounts of ascorbic acid and uric acid may cause a slightly higher result than the actual glucose level.

- High concentrations of acetaminophen and other reducing substances in the blood may cause inaccurately high results.
- Blood samples that contain a high concentration of dissolved oxygen may lower the test result.
- Antiglycolytics and anticoagulants in blood samples may affect the test results.

Hematocrit Effect

The effect of sample hemoglobin variation on the G4 device was tested experimentally by preparing samples of three known hematocrit values (20, 40% (normal) and 60%) at four blood glucose concentrations in replicates of ten. The YSI 2300 STAT Plus served as the reference instrument. The difference, average, SD, % CV and bias were calculated. The results from the hematocrit study met the sponsors' acceptance criteria.

Glucose range of 50 to 80 mg/dL	Hct 20	Hct 40	Hct 60
YSI Value	61.1	58.0	51.1
YSI Difference	3.1	0.0	-6.9
G4 Average (mg/dL)	72.4	60.9	56.8
SD	3.2	2.8	3.8
CV %	4.4	4.6	6.7
G4 Difference (mg/dL)	11.5	0.0	-4.1
Bias (mg/dL)	**8.4**	**0.0**	**2.8**

Glucose range of 100 to 180 mg/dL	Hct 20	Hct 40	Hct 60
YSI Value	122	116	106
YSI Difference	5.2	0.0	-8.6
G4 Average (mg/dL)	151.2	126.0	118.3
SD	4.5	3.9	2.0
CV %	3.0	3.1	1.7
G4 Difference (mg/dL)	20.0	0.0	-6.1
Bias (mg/dL)	**14.8**	**0.0**	**2.5**

Glucose range of 200 to 300 mg/dL	Hct 20	Hct 40	Hct 60
YSI Value	218	208	200
YSI Difference	4.8	0.0	-3.8
G4 Average (mg/dL)	242.2	211.1	208.0
SD	9.9	10.3	5.3
CV %	4.1	4.9	2.6
G4 Difference (mg/dL)	14.7	0.0	-1.5
Bias (mg/dL)	**9.9**	**0.0**	**2.4**

Glucose range of 301 to 500 mg/dL	Hct 20	Hct 40	Hct 60
YSI Value	416	410	388
YSI Difference	1.5	0.0	-5.4
G4 Average (mg/dL)	455.6	404.9	335.0
SD	9.2	16.3	8.9
CV %	2.0	4.0	2.7
G4 Difference (mg/dL)	12.5	0.0	-17.3
Bias (mg/dL)	**11.1**	**0.0**	**-11.9**

Altitude Effect

The monitors and strips were tested at 3050 meters to determine performance at low oxygen levels and low atmospheric pressures. This study used sixty -six G4 devices. The results were obtained and compared with sea level and YSI results taken in triplicate. The sponsor found that the percent error of the G4 device (both at sea level and 3050 meters) was less than 15%. The sponsor states that altitudes of up to 3050 meters do not affect the device.

Temperature and humidity study

The sponsor conducted temperature and humidity studies according to ISO 15197. Two studies that tested the strip results at specified temperature and humidity ranges were conducted. The temperatures tested were 8, 12, 20, 25, 38 and 42° C and the humidity tested were 35% and 85%.

The G4 device has available a temperature correction program that enables the device to obtain consistent results if obtain between 12 and 38° C. Blood with glucose concentrations of 55, 90, 145, 265 and 400 mg/dL (kept at 37° C) were tested in replicates of 10 at six different temperatures. The G4 device was tested for its ability to give consistent results if measurements are taken when humidity is between 35 and 85%. Blood with glucose concentrations of 150, 264 and 400 mg/dL (kept at 37° C) were tested in replicates of 10 in 2 different humid environments. The results for both studies are listed below.

Temperature	8° C	12° C	20° C	25° C	38° C	42°C
55 mg/dL						
Mean	Er3	54	53	55	58	Er3
SD	-	1.3	1.5	1.2	1.8	-
CV%	-	2.5	2.8	2.2	3.0	-
90 mg/dL						
Mean	Er3	89	87	89	89	Er3
SD	-	2.5	1.9	2.1	2.3	
CV%	-	2.8	2.2	2.3	2.6	
145 mg/dL						
Mean	Er3	144	146	145	147	Er3
SD	-	3.2	3.9	3.0	4.6	-
CV%	-	2.2	2.7	2.1	3.1	-
265 mg/dL						
Mean	Er3	266	268	261	267	Er3
SD	-	7.0	6.3	5.6	5.7	-
CV%	-	2.6	2.4	2.2	2.1	-
400 mg/dL						
Mean	Er3	400	391	400	412	Er3
SD	-	10.4	9.0	10.0	8.5	-
CV%	-	2.6	2.3	2.5	2.1	-

Humidity	35%	85%
145 mg/dL		
Mean	146	144
SD	4.9	4.3
CV%	3.4	3.0
265 mg/dL		
Mean	263	262
SD	6.1	4.6
CV%	2.3	1.8
400 mg/dL		
Mean	402	401
SD	7.2	5.2
CV%	1.8	1.3

The sponsor studies showed that the program of temperature correction allows users to obtain correct results between 12 and 38° C. The results also showed that the error message"Er3" works when the temperature is outside of the sponsors claimed range. The humidity results also showed that the device gives correct results when the measurements are taken within the sponsors claimed humidity range (35 – 85%).

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

Three separate clinical studies of the G4 device performance were performed.

A method comparison study was conducted with the G4 device against 2 predicates: LifeScan, Inc. SureStep and Roche Accu-check advantage. Three trained technicians collected capillary blood from 110 patients (68 men and 42 women). One of the results was excluded because the measurement fell outside the device range. The equation for the G4 versus the SureStep was y=1.0565x- 10.329 and r= 0.9923. The equation for the G4 versus the Accu-check was y=1.0224x + 1.4685 and r= 0.9852.

A consumer field study was performed in which the results obtained by 50 participants (in triplicate gave n=150) were compared to trained healthcare professional results and values obtained with YSI values. The study used test strips from 3 different lots. The lay-users ranged in age, education, and appropriately divided between female and male. The questionnaire and training materials were provided in English. Each participant performed their own finger stick and tested their blood using the instructions provided with the G4 system. After the user's self-test, the investigation site's trained healthcare professional performed another finger stick and tested the blood on the same meter. Capillary blood was collected and the YSI values were obtained.

3	50	y=0.83 + 19.58	0.9308	80 – 201	96	4

Lot #	**N**	**Healthcare Professional use vs. YSI**	**r value**	**Sample Range (mg/dL, by YSI)**	**Clark Error Grid**	
					A	B
Healthcare Results						
1	50	y=0.98x -1.73	0.9712	74 – 173	100	0
2	50	y=0.99x + 0.20	0.9858	63 – 160	100	0
3	50	y=0.96x + 2.62	0.9838	80 – 201	98	2
Lay User Results						
1	50	y=0.84x + 15.55	0.9306	74 – 173	96	4
2	50	y=0.96x + 5.65	0.9411	63 – 160	98	2

An additional consumer study was conducted at three sites for a total of 304 samples. Site one and site two compared results obtained from patients who tested themselves using the G4 meter to YSI values (224 and 71 samples respectively). Site three compared results obtained from patients who tested themselves using the G4 meter to the values obtained from the Accu-check Active meter (109 samples).

Site #	**N**	**Healthcare Professional use vs. YSI or Accu-check**	**r value**	**Sample Range (mg/dL, by G4)**	**Clark Error Grid**	
					A	B
1	244	y=1.02x - 1.816	0.989	53 to 342	98.2	0.8
2	71	y=1.08x - 9.19	0.989	47 to 475	100	0
3	109	y=1.02x +1.33	0.985	75 to 429	99	1

An alternate site study was conducted to determine the ability of the device to give forearm results consistent with finger stick results. Test results from the forearm site sampling and fingertip sampling (taken within 5 minutes apart) were compared with the test results obtained with the YSI instrument (n=114). Results are shown in the chart below. Finger stick ranges were 47 to 475 mg/dL, forearm ranges were 55 to 491 mg/dL and YSI values ranged from 50 to 425 mg/dL.

	Equation	R	Clark Error Grid (%)	
			A	B
Finger vs. YSI	y=1.06x-5.75	0.9812	98	2
Forearm vs. YSI	y=1.06x + 1.26	0.9827	95	5
Finger vs. Forearm	y=0.97x + 11.47	0.9770	96	4

The Clark Error Grid A and B regions are defined as: Zone A-Clinically accurate, within +/- 20% of the laboratory and Zone B-Error greater than +/- 20%, but would lead to begin or no treatment.

An accuracy study was conducted on capillary blood samples from 152 patients samples ran in duplicate. In accordance with the ISO 15197, seven ranges of glucose concentrations were covered with the correct percentage of samples. The glucose results obtained with the G4 were compared with the YSI 2300 STAT Plus values.

The sponsor based its accuracy specifications on the ISO International Standard 15197 which states that the minimum acceptable accuracy for results shall be 95% of the individual results shall fall within +/- 15 mg/dL at glucose concentrations less than 75 mg/dL and within +/- 20% at glucose concentrations greater than 75 mg/dL. Accuracy results (n= 304) are shown below.

Accuracy results for glucose concentration <75 mg/dL			
Within +/- 5 mg/dL	Within +/- 10 mg/dL	Within +/- 15 mg/dL	
40/44 (90.9%)	44/44 (100 %)	44/44 (100%)	
Accuracy results for glucose concentration > 75 mg/dL			
Within +/- 5 mg/dL	Within +/- 10 mg/dL	Within +/- 15 mg/dL	Within +/- 20 mg/dL
178/260 (68.5%)	232/260 (89.2%)	248/260 (95.4%)	259/260 (99.6 %)

The samples ranged from 26 to 530 mg/dL (n=304) and the regression equation was Y=1.052 x – 4.6044 and R2= 0.994 with y=G4 and x=YSI reference method.

b. Matrix comparison:

Not applicable

3. Clinical studies:

a. Clinical Sensitivity:

Not applicable

b. Clinical specificity:

Not applicable

c. Other clinical supportive data (when a. and b. are not applicable):

The sponsor conducted a Flesch Kincaid Readability test and the results are in the chart below.

Document	**Grade Level**
G4 Communication Program	7.52
G4 Test Strip Insert	7.74
G4 Owners Manual	6.63
G4 Quick Reference	4.94
G4 Control Manual	7.46

4. Clinical cut-off:

Not applicable

5. Expected values/Reference range:

The normal glucose range for a non-diabetic is less than 110 mg/dL before a meal. The normal average bedtime glucose range should be less than 120 mg/dL. The sponsor

instructs the patient to discuss and determine individual recommended target blood glucose range with their physician.

The sponsor references the following: Diabetes Care, Volume 25, Supplement 1, January 2002.

N. Instrument Name:

G4 Meter Device

O. System Descriptions:

1. Modes of Operation:

   Test strips can only be used once. Users must replace the strip before taking additional readings.

2. Software:

   FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types:

   Yes __X_____ or No _____

3. Specimen Identification:

   There is no sample identification function with this device. Samples are applied directly to the test strip as they are collected.

4. Specimen Sampling and Handling:

   This device is intended for use with fresh capillary whole blood. Since the sample is applied directly to the test strip there are no special handling or storage issues.

5. Calibration:

   Each bottle of test strips has a test code on the vial. The code numbers on the G4 Meter display and G4 Test strips must match. The user must compare the code number printed on the test strip vial with the user interface of the meter.

6. Quality Control:

   The company provides two levels of glucose control solutions (also sold separately) with the device. To access the accuracy of the meter in combination with the strips, glucose control solutions that contain a known amount of glucose are tested with the meter. The company also provides a check strip to help users determine if the meter is functioning

properly. If control results fall outside these ranges, the user is referred to a list of troubleshooting steps or to call 866-216-5308.

P. Other Supportive Instrument Performance Characteristics Data Not Covered In The "Performance Characteristics" Section above:

Not Applicable

Q. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

R. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.